



## Cellular and Tissue Composition of the Pancreas in Individuals with or at Increased-Risk for Type 1 Diabetes

### AUTHORS

***Xiaohan Tang<sup>1,2</sup>, Irina Kusmartseva<sup>1</sup>, Shweta Kulkarni<sup>1</sup>, Amanda Posgai<sup>1</sup>, Stephan Speier<sup>3,4,5</sup>, Desmond A. Schatz<sup>6</sup>, Michael J. Haller<sup>6</sup>, Martha Campbell-Thompson<sup>1</sup>, Clive H. Wasserfall<sup>1</sup>, Bart O. Roep<sup>7</sup>, John S. Kaddis<sup>7,8</sup>, Mark A. Atkinson<sup>1,6</sup>.***

<sup>1</sup> Department of Pathology, Immunology and Laboratory Medicine, Diabetes Institute, University of Florida, Gainesville, FL, USA

<sup>2</sup> Department of Metabolism and Endocrinology, The Second Xiangya Hospital, Central South University, Changsha, Hunan, China

<sup>3</sup> Paul Langerhans Institute Dresden (PLID) of the Helmholtz Zentrum München at the University Clinic Carl Gustav Carus of Technische Universität Dresden, Helmholtz Zentrum München, Neuherberg, Germany

<sup>4</sup> Institute of Physiology, Faculty of Medicine, Technische Universität Dresden, Germany

<sup>5</sup> German Center for Diabetes Research (DZD), München-Neuherberg, Germany

<sup>6</sup> Department of Pediatrics, College of Medicine, University of Florida, Gainesville, FL, USA

<sup>7</sup> Department of Diabetes Immunology, Diabetes and Metabolism Research Institute, City of Hope/Beckman Research Institute, Duarte, CA, USA

<sup>8</sup> Department of Diabetes and Cancer Discovery Science, Diabetes and Metabolism Research Institute, City of Hope/Beckman Research Institute, Duarte, CA, USA

### PURPOSE

Once thought a disease primarily affecting  $\beta$ -cells, emerging evidence suggests that type 1 diabetes (T1D) affects both the endocrine and exocrine pancreatic compartments. However, a quantitative description of acinar, ductal, and non-endocrine/non-exocrine tissues within the human T1D pancreas is lacking.

### METHODS

We utilized HALO image analysis software to analyze scanned whole human pancreas cross-sections from nPOD donor cohort, stained for insulin and glucagon by IHC as well as H&E, from the head, body, and tail regions. We characterized pancreatic exocrine and endocrine tissue compositions by quantifying the proportion of endocrine, acinar, and ductal/other areas as well as acinar and endocrine cell density, and size in subjects with or at-risk for T1D as well as controls without diabetes.

### SUMMARY OF RESULTS

In insulin- pancreata with T1D, overall acinar area was reduced, whereas ductal, vessel, fibrotic, adipose and nerve tissue areas were greater in comparison to either non-diabetic group. In contrast, acinar area in insulin+ pancreata from subjects with T1D was similar to both non-diabetic groups; yet, cell size was smaller and cell density was higher in comparison to non-diabetic autoantibody negative individuals. Endocrine tissue area and cells were smaller in T1D pancreata compared to either non-diabetic group. The main

pancreatic duct was thicker and occupied area smaller in the tail vs. body region, independent of disease.

### **CONCLUSIONS**

These data provide novel insights into anatomical differences in T1D pancreata and suggest that while such variations could conceivably precede diagnosis, the loss of residual  $\beta$  cells following onset likely has an influence on the exocrine compartment.